

REMARKS***Status of the Application:***

This paper is filed in response to the Final Office Action mailed on August 20, 2008 (hereinafter, the "Office Action"). At the time the Office Action was mailed, claims 1-4, 6, 8-14, 17-18, and 26-27 were pending in the application. Claims 12-14 were withdrawn without prejudice. Claims 5 and 19-25 were previously cancelled. In the instant response, claim 1 has been amended. Applicant reserves the right to pursue the cancelled claims in a continuing application.

Support for the amendment to claim 1 can be found, for example in paragraph [0093-0094] of the specification (page 19, second and third full paragraphs of the English translation of the PCT application). Therefore, upon entry of the instant amendment, claims 1-4, 6, 8-11, 17-18, and 26-27 will be before the Examiner for consideration.

Withdrawal of objections and/or rejections

Applicant thanks the Examiner for withdrawal of all of the previous objections and rejections in the instant case.

Objection to claims

The Office Action has objected to claim 1 for reciting "one or more types of tissue cells" instead of "myocardial cells." Applicant thanks the Examiner for the careful reading of the claims. Applicant has amended the claim as suggested. The objection is overcome. Withdrawal of the objection is respectfully requested.

Rejections Under 35 U.S.C. § 103:

The Office Action has rejected claims 1-4, 6, 8-11, 17-18, and 26-27, all of the claims under examination in the instant application, as allegedly being unpatentable over Kosaka et al. (hereinafter Kosaka) and Harutu et al. (hereinafter Harutu) in view of Rezai et al. (hereinafter Rezai).

Applicant respectfully disagrees and traverses the rejection.

Kosaka and Haruta describe that iris pigmented epithelial cells of a chicken or a mammal were successfully isolated and cultured. Rezai describes a culturing and transferring method of iris pigmented epithelial cells.

The Examiner asserts in the Office Action that Rezai discloses a spheroid model that has resistance to dedifferentiation, and further asserts that Rezai suggests that a pluripotent stem cell can be obtained from iris pigmented epithelial cells by the floated coagulated mass culturing technique.

Applicant respectfully disagrees.

In the claimed method for producing myocardial cells as recited in claim 1 of the present invention, the pluripotent stem cells obtained in step (iv) are in a state which has not been subjected to differentiation to specific tissues, and it can be said that the pluripotent stem cells at step (iv) are non-differentiated cells which can be differentiated into various types of cells (see paragraph [0011] (lines 10 to 15 of page 3 of the English specification) and paragraph [0901] (lines 22 to 25 of page 3 of the English specification) of the PCT specification).

Rezai discloses a culturing condition for high-density culturing for stabilization of iris pigmented epithelial cells. More specifically, in Rezai, after the iris pigmented

epithelial cells are dissociated, the iris pigmented epithelial cells are coagulated and cultured at a high density to stabilize and maintain as the iris pigmented epithelial cells.

That is to say, if the dedifferentiation of the iris pigmented epithelial cells are suppressed according to the culturing method of the iris pigmented epithelial cells described in Rezai, it can be considered that Rezai teaches away from the present invention. Therefore, the culturing method of the iris pigmented epithelial cells described in Rezai is fundamentally different from the "floated coagulated mass culturing technique" of the present invention.

Without agreeing with the Examiner and to progress the prosecution of the application, Applicant has amended claim 1, adding the limitation of the "floated coagulated mass culturing technique" so that the floated coagulated mass culturing technique is more clearly distinguished from the culturing method disclosed in Rezai.

The floated coagulated mass culturing technique described in instantly amended claim 1 uses serum-free medium and an N2 supplement as a culturing medium, and the cultures the isolated iris pigmented epithelium are cultured with rotation (e.g., on a rotary shaker). As noted in the Office Action, each Kosaka, Haruta, and Rezai culture cells in the presence of fetal bovine serum. Moreover, there is no teaching or suggestion to modify the growth media, or in what manner the growth media should be modified to arrive at the instantly claimed invention.

The instantly claimed invention is neither disclosed nor suggested in Rezai. The deficiencies of Rezai cannot be overcome by the teachings of the combination of Kosaka and Haruta.

Therefore, the present invention cannot be arrived by combining the cited references, none of which disclose or suggest the floated coagulated mass culturing technique described in the amended claim 1 of the present invention.

For at least the reasons set forth herein, Applicants respectfully submit that a *prima facie* case of obviousness has not been established under the requirements of 35 U.S.C. § 103(a). To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)). Second, there must be a reasonable expectation of success. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicants' disclosure. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974).

The invention of the present application carries out clonal growth from one cell by culturing the iris pigmented epithelial cells dissociated using a trypsin solution, by the floated coagulated mass culturing technique with rotation from a relatively low initial number of cells. This low density culturing method deprives the iris pigmented epithelial cells of its properties as pigmented epithelium and "unpigments" the iris pigmented epithelial cells, thereby attaining pluripotent stem cells through the selective culturing. The pluripotent stem cells are differentiable to various types of tissue cells. This point is demonstrated in the attached manuscripts written by one of the inventors of the instant application (Reference Document 1: Developmental Biology 289 (2006) 243-252, Reference Document 2: Developmental Biology 304 (2007) 433-446, copies enclosed) after the present application was filed. Further culturing of the obtained stem cells under differentiation inducing condition of the instantly claimed invention attains an unexpected effect such that myocardial cells are obtained from the stem cells.

Therefore, the invention described in the amended claim 1 and the dependent claims thereof are not attainable even by combining the cited references, and thereby being non-obvious over the cited references.

Therefore, the invention as claimed cannot be considered obvious in view of any of the cited references. Withdrawal of the rejection is respectfully requested.

Conclusion:

In view of the amendments and arguments presented herein, Applicants submit that the claims are in condition for allowance.

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Respectfully submitted,

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